

# ***Aspergillus fumigatus* protein phosphatase PpzA is involved in iron assimilation, secondary metabolite production, and virulence.**

Manfioli AO, de Castro PA, Dos Reis TF, Dolan S, Doyle S, Jones G, Riaño Pachón DM, Ulaş M, Noble LM, Mattern DJ, Brakhage AA, Valiante V, Silva-Rocha R, Bayram O, Goldman GH (2017) *Aspergillus fumigatus* protein phosphatase PpzA is involved in iron assimilation, secondary metabolite production, and virulence. *Cell Microbiol* 19(12),

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## **Abstract**

Metal restriction imposed by mammalian hosts during an infection is a common mechanism of defense to reduce or avoid the pathogen infection. Metals are essential for organism survival due to its involvement in several biological processes. *Aspergillus fumigatus* causes invasive aspergillosis (IA), a disease that typically manifests in immunocompromised patients. *A. fumigatus* PpzA, the catalytic subunit of protein phosphatase Z (PPZ), has been recently identified as associated with iron assimilation. *A. fumigatus* has two high affinity mechanisms of iron acquisition during infection: reductive iron assimilation (RIA) and siderophore-mediated iron uptake. It has been shown that siderophore production is important for *A. fumigatus* virulence, differently to the reductive iron uptake system. Transcriptomic and proteomic comparisons between  $\Delta$ ppzA and wild-type strains under iron starvation showed that PpzA has a broad influence on genes involved in secondary metabolism. LC-MS under standard and iron starvation conditions confirmed that the

$\Delta$ ppzA mutant had reduced production of pyripyropene A (PPA), fumagillin, fumiquinazoline A, TAFC, and helvolic acid. The  $\Delta$ ppzA was shown to be avirulent in a neutropenic murine model of invasive pulmonary aspergillosis. PpzA plays an important role at the interface between iron starvation, regulation of SM production and pathogenicity in *A. fumigatus*.

## Beteiligte Forschungseinheiten

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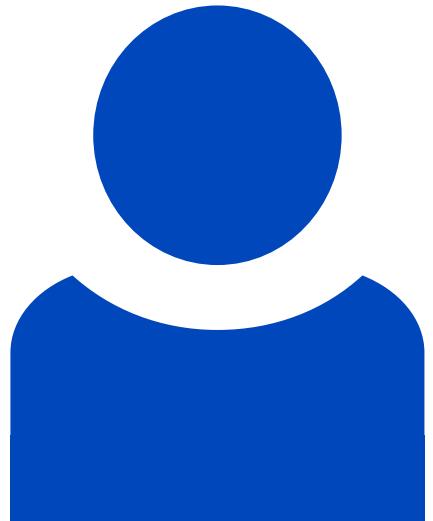
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